Sibling similarities in the tempo of human tooth mineralization

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Abstract

The extent of tooth mineralization is a useful estimate of a child's physiological age; it reflects the rate at which the child is developing towards maturity. As it is not known to what degree dental age is regulated by the genotype, this investigation estimated familial resemblance in the tempo of tooth mineralization. Panoramic radiographs of the children in 185 sibships were scored for stages of tooth formation, and dental age was calculated from sex-specific standards. Intraclass correlations of mineralization tempo were computed for maxillary and mandibular canines, premolars, second molars, and third molars. Correlations of mineralization tempo were significantly different than zero for all 10 teeth and ranged from 0.17 (SE = 0.06) for the mandibular second molar to 0.43 (SE = 0.05) for the mandibular second premolar. Intraclass correlations increased significantly when multiple teeth were used to more comprehensively define each child's dental age. Using an unweighted average of all 10 tooth types yielded a correlation of 0.41 (SE = 0.05). It appears, then, that a considerable proportion of the total variability in tooth-mineralization rate can be attributed to transmissible effects operating in the population under investigation. © 1998 Elsevier Science Ltd. All rights reserved.

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1. Introduction

While maturational events normally occur in a uniform sequence during a child's growth, the chronological age at which each event occurs varies among children. The statement that a boy is 13 years old is vague from the standpoint of growth and development. In order to determine his level of physiological development and to anticipate his remaining growth potential, it is more relevant to know how his biological age compares with his chronological age. The concept of biological age was first introduced by Crampton (1908) to more precisely estimate the degree of maturation of a growing child. Biological age is the average chronological age—obtained from population-specific standards—at which a child's existing level of maturation occurs, regardless of his or her actual chronological age.

A child's rate of growth may be advanced, normal, or delayed compared to age- and sex-specific population norms. This trait was termed the tempo of growth by Franz Boas, and the tempo has been shown to remain relatively constant throughout the growth of a child (Boas, 1932; 1933; 1935). Tanner (1962; 1963) described the tendency of growth to return to its original path as target-seeking behaviour. He proposed that factors affecting the tempo of growth be considered separately from factors affecting the size, shape, and body composition of a child, as environmentally produced changes in growth tempo do not necessarily reflect changes in final size or shape. For example, both undernutrition and severe illness may delay statural growth, as shown by the effects of famine associated with war on incremental growth changes.
(e.g. Howe and Schiller, 1952), but the undernourished or ill child can exhibit a catch-up period when normal nutrition and health are restored, and normal body dimensions will most probably be attained eventually (Prader et al., 1979). Control of the tempo of growth seems to be modulated by the child’s genotype.

Extensive data on population differences in growth rate between national and racial groups were compiled by Eveleth and Tanner (1990). Differences between the major human races are de facto evidence of a genetic influence on the tempo of growth.

Positive and statistically significant Pearson product-moment correlation coefficients between family members in the tempo of skeletal maturation, statural growth (e.g., Boas, 1932), and dental maturation and emergence (Hatton, 1955; Garn et al., 1960) have been reported. The sharing of genes in common is assumed to contribute to this familial similarity; however, common environmental conditions within families can contribute to the positive associations (Garn et al., 1979).

Our purpose now was to assess genetic influence on the tempo of growth as gauged by intraclass correlations calculated between full siblings of the rate of tooth mineralization.

2. Materials and methods

Panoramic radiographs were studied from children in 185 sibships. The radiographs were from the pretreatment records of routine dental patients at the College of Dentistry, University of Tennessee, Memphis, and from dental specialists in the local community. Of the sibships studied, 175 were composed of two siblings, eight consisted of three siblings, and two consisted of four siblings. There were 382 individuals, 174 males and 208 females, ranging in age from 4.2 to 15.5 years, with a mean of 9.5 years (SD = 2.5 years).

As shown in Fig. 1, there was an approximately uniform distribution of the sample through the age interval of 6 to 14 years. No exclusionary criteria were used to eliminate children within the normal range of variation; however, those with evidence of developmental abnormalities as shown by their medical history were excluded. Within each panoramic radiograph, individual teeth were excluded if their deciduous predecessors were prematurely missing, over-retained, or pulpally involved, as these conditions can affect the rate of development of the succedaneous tooth (e.g., Fanning, 1962; Loey, 1989).

Although tooth mineralization is a continuous process, from initial mineralization of the cusp tip to the completion of apex, it can be divided into discrete, repeatably identifiable stages to simplify study. The ordinal scale developed by Moorrees et al. (1963) was used here to quantify the extent of tooth mineralization. All developing permanent teeth were scored, but there were too few early-forming teeth (I1, 12, M1) for analysis, so 10 instead of all 16 tooth types are described here. Each tooth was scored as the highest
stage that it had attained. There was no interpolation or selection of the “closest” grade. Given the strong left-right concordance of tooth development (e.g., Demirjian, 1978) it was redundant to score all teeth. Instead, the tooth with the clearer radiographic image was scored for each left-right pair of teeth.

Double determinations on 100 cases produced identical readings for 92% of the teeth, with no difference exceeding one stage. This level of concordance compares favourably with earlier reports (Fanning, 1961; Grom, 1962; Harris and McKee, 1990).

Mineralization tempo was assessed using three steps for each scorable tooth as follows. (1) The formation stage of the tooth was used to find the average chronological age at which normal children achieve that stage using the sex-specific norms of Harris and McKee (1990). This was termed observed age (OA). (2) The chronological age of the child was then used to find the stage of tooth formation expected if he or she were growing at a normal rate. The corresponding age (from the Harris-McKee norms) for that stage was termed expected age (EA). (3) By comparing expected age (EA) to observed age (OA), the degree of advancement or delay in mineralization rate was calculated (i.e., tempo = OA - EA). “Tempo” is the relative dental age for that tooth. A positive tempo denoted an early maturer; a negative value denoted a late maturer. This procedure was used to generate a tooth-specific dental age for each scorable tooth type in each child.

Dental age is normally calculated from all scorable tooth types (e.g., Moorrees et al., 1963; Demirjian et al., 1973; Loey and Goldberg, 1996) to exploit all of the available dental information. The two options are to calculate tooth-specific and multiple-tooth estimates of a child’s dental age, which are analogous to the bone-specific versus the atlas methods of estimating hand-wrist bone age (Greulich and Pyle, 1959). Arithmetic averages of the residuals (OA - EA) of four tooth combinations within each child were tested: (1) maxillary and mandibular canines, (2) maxillary and mandibular first and second premolars, (3) maxillary and mandibular second and third molars, and (4) mandibular and mandibular canines, first and second premolars, and second and third molars.

Intraclass correlations (ri) of mineralization tempo were computed using procedures described by Falconer (1989). In brief, ri is the ratio of the variance among sibships to the total variance.

\[ r_i = \frac{s_{ib}^2}{s_{ib}^2 + s_{wb}^2} \]

where \( s_{ib}^2 \) and \( s_{wb}^2 \) are the between- and within-sibship variance, respectively. When \( s_{wb}^2 \) is small—so brothers and sisters within sibships are similar for the trait being studied—\( s_{ib}^2 \) will be comparatively large and \( r_i \) will be high. The intraclass correlation is the interclass correlation that would be observed if the classes were indefinitely large and the average correlation between a member of a class and another member of the same class were calculated (Kempthorne, 1957). The SAS statistical package, specifically the general linear-model routines, were used to calculate the sums of squares (SAS Institute Inc., 1989). Weighted sibship size, \( n_s \), was

\[ n_s = \frac{1}{a - 1} \left( \sum n_i - \frac{\sum n_i^2}{\sum n_i} \right) \]

where \( a \) is number of sibships and \( n_i \) is number of siblings in sibship \( i \) (Sokal and Rohlf, 1981). Standard error of \( r_i \) was calculated from formulae in Swiger et al. (1964).

3. Results

Intraclass correlations for the 10 tooth types are listed in Table 1. The raw data are observed-minus-expected differences or “temps” of growth, so results address the relative rates of growth within and among sibships. Each of the 10 correlations was significantly different from zero, so the temps of tooth formation are significantly more alike among siblings than among sibs. It is assumed that this similarity in growth rates is due primarily to the fact that siblings (and other first-degree relatives) share half of their genes in common by descent. Additionally, though, effects of living together (i.e., environmental covariation) may enhance the observed phenotypic similarity (e.g., Kempthorne and Osborne, 1961). Correlations ranged from 0.17 for the mandibular second molar to 0.43 for the mandibular second premolar. No mesiodistal gradient or maxillary-mandibular difference was evident. Also, no difference between early- and late-forming teeth was detected.

Intraclass correlations using multiple-tooth combinations (Table 1) yielded values significantly different from zero; indeed, the familial influences appeared higher than for calculations using individual teeth, and a Wilcoxon sign-rank test (Siegel and Castellan, 1988) showed this to be true (\( p < 0.02 \)). The increased reliability of using multiple teeth to calculate dental age (e.g., Demirjian et al., 1973) resulted in coefficients ranging from 0.32 for the combination of all four molars to 0.45 for the combination of all four premolars. When all 10 tooth types were combined, the correlation coefficient was 0.41, with 95% confidence limits of 0.32 and 0.51.
Table 1

<table>
<thead>
<tr>
<th>Tooth</th>
<th>n_i</th>
<th>total n</th>
<th>Sibships n</th>
<th>F-ratio sibship</th>
<th>( r_i )</th>
<th>SE</th>
<th>L_1</th>
<th>L_2</th>
</tr>
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<tbody>
<tr>
<td><strong>Mandibular Teeth</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canine</td>
<td>1.93</td>
<td>336</td>
<td>174</td>
<td>1.89**</td>
<td>0.32</td>
<td>0.06</td>
<td>0.20</td>
<td>0.43</td>
</tr>
<tr>
<td>First premolar</td>
<td>1.96</td>
<td>361</td>
<td>184</td>
<td>2.18**</td>
<td>0.38</td>
<td>0.05</td>
<td>0.27</td>
<td>0.48</td>
</tr>
<tr>
<td>Second premolar</td>
<td>2.02</td>
<td>373</td>
<td>185</td>
<td>2.53**</td>
<td>0.43</td>
<td>0.05</td>
<td>0.33</td>
<td>0.53</td>
</tr>
<tr>
<td>Second molar</td>
<td>2.05</td>
<td>379</td>
<td>185</td>
<td>1.42**</td>
<td>0.17</td>
<td>0.06</td>
<td>0.05</td>
<td>0.29</td>
</tr>
<tr>
<td>Third molar</td>
<td>1.47</td>
<td>152</td>
<td>103</td>
<td>1.58**</td>
<td>0.28</td>
<td>0.12</td>
<td>0.04</td>
<td>0.53</td>
</tr>
<tr>
<td><strong>Maxillary Teeth</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Canine</td>
<td>1.91</td>
<td>339</td>
<td>177</td>
<td>2.36**</td>
<td>0.42</td>
<td>0.05</td>
<td>0.31</td>
<td>0.52</td>
</tr>
<tr>
<td>First premolar</td>
<td>1.95</td>
<td>302</td>
<td>155</td>
<td>1.83**</td>
<td>0.30</td>
<td>0.06</td>
<td>0.18</td>
<td>0.42</td>
</tr>
<tr>
<td>Second premolar</td>
<td>1.91</td>
<td>332</td>
<td>174</td>
<td>2.04**</td>
<td>0.35</td>
<td>0.06</td>
<td>0.24</td>
<td>0.47</td>
</tr>
<tr>
<td>Second molar</td>
<td>1.93</td>
<td>343</td>
<td>178</td>
<td>1.81**</td>
<td>0.30</td>
<td>0.06</td>
<td>0.18</td>
<td>0.42</td>
</tr>
<tr>
<td>Third molar</td>
<td>1.42</td>
<td>164</td>
<td>115</td>
<td>1.90**</td>
<td>0.29</td>
<td>0.11</td>
<td>0.17</td>
<td>0.60</td>
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<tr>
<td><strong>Combination of Teeth</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both canines</td>
<td>1.98</td>
<td>352</td>
<td>178</td>
<td>2.23**</td>
<td>0.38</td>
<td>0.05</td>
<td>0.28</td>
<td>0.49</td>
</tr>
<tr>
<td>All 4 premolars</td>
<td>2.05</td>
<td>380</td>
<td>185</td>
<td>2.67**</td>
<td>0.45</td>
<td>0.05</td>
<td>0.36</td>
<td>0.54</td>
</tr>
<tr>
<td>All 4 molars</td>
<td>2.06</td>
<td>381</td>
<td>182</td>
<td>1.98**</td>
<td>0.32</td>
<td>0.05</td>
<td>0.22</td>
<td>0.43</td>
</tr>
<tr>
<td>All 10 teeth</td>
<td>2.06</td>
<td>382</td>
<td>185</td>
<td>2.44**</td>
<td>0.41</td>
<td>0.05</td>
<td>0.32</td>
<td>0.51</td>
</tr>
</tbody>
</table>

1 Columns are: weighted size of sibships (\( n_i \)); total number of individuals; number of sibships; F-ratio testing for a significant sibship effect; intraclass correlation coefficient (\( r_i \)); standard error of \( r_i \); and the lower and upper bounds (\( L_1, L_2 \)) of the 95% confidence limits of \( r_i \).

- **0.01 < p < 0.05.**
- **0.05 < p < 0.01.**

4. Discussion

Familial similarities in physical traits, such as craniodimetrics and tooth-crown diameters, have shown that a majority of the phenotypic variation is accounted for by the individuals' genotype (e.g., Susanne, 1977; Townsend and Brown, 1978; Harris and Johnson, 1991). Such studies have disclosed discernible levels of familial predisposition for the size (or amount of growth) of somatic structures. The major focus of the present study was to test for familial association in the rate of growth, specifically, the tempo of tooth mineralization. The median correlation for the 10 individual teeth was 0.32, and the correlation for all 10 teeth was 0.41. These are rather high when one recalls that the upper limit for a correlation between full siblings under the assumption of complete control by additive genes is 0.50 (Falconer, 1989). Heritability, the proportion of the phenotypic variation attributable to genotypic variation (\( V_G/V_P \)), is twice the intraclass correlation (Fisher, 1918; Falconer, 1989). For the composite of all 10 teeth, then, heritability would be 82%, which is rather high—though this estimate may be inflated by environmental covariance. That is, siblings share similar prenatal and postnatal environments and phenotypic similarity arising from shared environmental experiences will inflate full-sib covariances to an indeterminate degree. For example, Bailit and Sung (1968) found significant negative associations between the tempo of dental development and birth order and maternal age. Consequently, this estimate of a transmissible component might best be viewed as an upper limit of the true level of genetic control.

Researchers have compared the effects of several environmental factors on tooth-mineralization rate to the corresponding effects on somatic development (Garr et al., 1965a,b; 1974; 1986). Garr et al. (1974) evaluated the association between socioeconomic status and the relative advancement or delay in tooth-emergence rate and found a delay in tooth emergence in lower income groups. However, the average delay was only about 2 months, which was much less than that observed for hand-wrist ossification timing in the same sample (Garn et al., 1965a) showed that tooth mineralization was delayed in hormonal deficiencies such as hypothyroidism and hypopituitarism, but that this delay was approximately half as much as the delay in skeletal development. Hormonal excesses such as sexual precocity were associated with advanced tooth formation and emergence, but dental advancement
occurred to a lesser degree than skeletal development. Overall, environmental agents have some effect on the rate of tooth development, but these effects are substantially smaller than the corresponding effects on skeletal and general somatic development. It appears that dental development is sheltered from the environmental factors known to affect skeletal development and stature growth, even though there is a significant positive association between bone age and dental age, at least in developmentally normal children (e.g., Lilleheik and Lundberg, 1971; Sierra, 1987).

As the level of genetic control for rate of tooth formation is not random, there must be some biological advantage for well-regulated velocities of development. What adaptive value might there be? Growth slows in the undernourished or ill child, then exhibits a catch-up period when normal nutrition and health are restored (Prader et al., 1963; Wilson, 1979; Mosier, 1989). Except in the cases of prolonged malnourishment or severe chronic illness, normal body dimensions will likely be attained.

Consider that humans probably evolved in small tribal communities, most of the time nomadic, following a potentially precarious food supply. In such an environment, where nutrition was never assured, the capacity to restrict growth during times of food shortage then catch up when food supply was resumed allowed survival in the face of a fluctuating food supply (Bogin, 1988). A species unable to vary its growth tempo in the face of these fluctuations would probably have become extinct. Thus, a delay in general somatic growth would be advantageous during periods of decreased food supply.

In contrast, there is no apparent benefit to such a delay in dental maturation during periods of decreased food supply. In fact, a delay in tooth development as a result of malnourishment might be disadvantageous. Due to the abrasive diet, the dentition of early man was used with vigour, and an intact dentition was probably essential to survival. Delay in the development and emergence of permanent teeth during times of food shortage would limit the ability to gain nourishment when food became available. It is possible that, as a result of the necessity to sustain dental development in the face of fluctuations in nutrition, development of the teeth remained sheltered from the environmental variability that affects general somatic growth.

In summary, a considerable proportion of the total variability in tooth mineralization rate can be attributed to genetic effects operating in the population under investigation. While previous research has shown that the size of somatic structures is genetically regulated, we show that the rate of development of these structures also is under ponderable genetic control.

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References